doi: 10.13241/j.cnki.pmb.2019.24.042

多囊卵巢综合征患者胰岛素抵抗和胰岛β细胞分泌功能与氧化应激的相关性研究*

孙 林[1] 王海燕[2△] 王美仙[2] 王化丽[1] 刘莉娜[1]

（1 大连市妇幼保健院暨大连医科大学附属妇产医院,生殖保健中心 辽宁 大连 116030;
2 大连市妇女儿童医疗中心,生殖与遗传中心 辽宁 大连 116033）

摘要 目的:探讨多囊卵巢综合征(PCOS)患者胰岛素抵抗(IR)和胰岛β细胞分泌功能与氧化应激的相关性。**方法:**选择122名在大连市妇幼保健院生殖保健中心就诊的PCOS患者82例,包括IR组42例和非IR组40例,同期选取单纯因男性因素不育而月经规律、内分泌激素正常的对照组患者40例。检测空腹血糖(FBG)、空腹胰岛素(FINS)水平,测定血清活性氧(ROS)和丙二醛(MDA)含量以评价机体氧化应激,测定血清总抗氧化能力(TAC)和超氧化物歧化酶(SOD)含量评价机体的抗氧化能力,使用稳态模型评价机体的胰岛素抵抗(HOMA-IR)和胰岛β细胞分泌功能(HOMA-β)。**结果:**PCOS胰岛素抵抗组患者身体质量指数(BMI)、促黄体素(LH)、黄体生成激素/卵泡生成激素(LH/FSH)、睾酮(T)、FBG、FINS和HOMA-IR显著高于非IR和对照组,而HOMA-β显著低于非IR和对照组，差异均有统计学意义（$P<0.05$）;PCOS胰岛素抵抗组血清ROS和MDA含量较非IR组和对照组显著升高($P<0.05$),非IR组ROS含量显著高于对照组($P<0.05$),而非IR组和对照组MDA含量相比差异无显著性($P>0.05$);PCOS胰岛素抵抗组血清TAC和SOD含量较非IR组和对照组显著降低($P<0.05$),而非IR组血清TAC和SOD含量低于对照组,但差异无显著性($P>0.05$)。PCOS患者HOMA-IR与体质指数(BMI)及血清ROS和MDA水平呈正相关$P<0.01$),与血清TAC和SOD活性呈显著负相关($P<0.05$)。**结论:**氧化应激与PCOS患者胰岛素抵抗密切相关,可能在其胰岛素抵抗发生发展进程中发挥着重要的作用。

关键词:多囊卵巢综合征(PCOS);胰岛素抵抗(IR);胰岛β细胞分泌功能;氧化应激

中图分类号:R711.75 **文献标识码:**A **文章编号:**1673-6273(2019)24-4780-05

Pancreatic β Cell Secretory Function and Oxidative Stress with the Insulin Resistance in Patients with Polycystic Ovary Syndrome Correlation*

SUN Lin[1], WANG Hai-yan[2△], WANG Mei-xian[2], WANG Hua-li[1], LIU Li-na[1]

(1 Dalian Maternal and Child Health Hospital and Obstetrics and Gynecology Hospital, Dalian Medical University, Dalian, Liaoning, 116030, China;

2 Dalian Women's and Children's Medical Center, Reproduction and Heredity Center, Dalian, Liaoning, 116033, China)

ABSTRACT Objective: To investigate the relationship between insulin resistance (IR) and pancreatic β cell secretory function and oxidative stress in patients with polycystic ovary syndrome (PCOS). **Methods:** A total of 122 participants were enrolled in the Reproductive Health Center of the Maternal and Child Health Hospital of Dalian, including 82 patients with PCOS (42 associated with IR and 40 without IR). The control group was 40 patients of the menstrual regularity and normal endocrine hormone were selected due to male factor infertility. The fasting blood glucose (FBG) and fasting insulin (FINS) were measured. The concentration of serum reactive oxygen species (ROS), malondialdehyde (MDA) and the activity of serum superoxide dismutase (SOD) and total antioxidant capacity (TAC) levels in all patients were measured to evaluate oxidative stress in the body. The homeostasis model was used to evaluate the body's insulin resistance (HOMA-IR) and pancreatic β cell secretory function (HOMA-β). **Results:** The body mass index (BMI), luteinizing hormone (LH), luteinizing hormone (LH/FSH), testosterone (T), FBG, FINS and HOMA-IR were significantly higher in the PCOS with insulin resistance group than those in the non-IR and control groups, while HOMA-β was significantly lower than those of the non-IR and control groups. The ROS and MDA in the PCOS IR group were significantly higher than that in the non-IR group and the control group ($P<0.05$), and the ROS content in the non-IR group was significantly higher than that in the control group ($P<0.05$). There was no significant difference in the MDA content between the non-IR group and the control group ($P>0.05$). The levels of serum TAC and SOD in the PCOS IR group were significantly lower than those in the non-IR group and the control group ($P<0.05$). The serum levels of TAC and SOD in the group were lower than those in the control group, but no significant difference was found($P>0.05$). HOMA-IR in patients with PCOS were positively associated with the body mass index (BMI), serum ROS and MDA levels($P<0.01$), and were negatively associated

* 基金项目:中华医学会临床医学科研专项基金项目(16020250641);辽宁省自然科学基金指导计划面上项目(20180550614)

作者简介:孙林(1976-),女,博士,主任医师,研究方向:不孕不育与辅助生殖,电话:13998611395,E-mail:chuyasu756@163.com

△ 通讯作者:王海燕(1978-),女,副主任医师,医学硕士,研究方向:生殖内分泌

(收稿日期:2019-07-23 接受日期:2019-08-17)

with the serum TAC and SOD activities (P<0.05). **Conclusion:** Oxidative stress is closely related to the insulin resistance in patients with PCOS, and may play an important role in the development of insulin resistance.

Key words: Polycystic ovary syndrome (PCOS); Insulin resistance (IR); Pancreatic β cell secretory function; Oxidative stress
Chinese Library Classification(CLC): R711.75 Document code: A
Article ID: 1673-6273(2019)24-4780-05

前言

多囊卵巢综合征(PCOS)是临床上常见的妇科疾病,患者主要表现为卵巢生成过量的雄激素,症状以月经量少、慢性无排卵、肥胖、多毛等为主,部分患者合并不孕[1]。其发生机制可能与多种因素有关,有研究表明氧化应激可能在许多 PCOS 患者中出现的不孕症和异质性疾病中起重要作用[2]。近年来,研究显示氧化应激在人类生育潜能中的作用备受学者关注。在机体正常状态下,氧化 / 抗氧化处于相对平衡的状态,机体活性氧(reactive oxygen species,ROS)生成过多和(或)机体抗氧化能力衰退等因素均可打破该平衡系统,致使细胞功能出现异常,诱发各类疾病的产生[3,4]。国内外关于 PCOS 不孕患者血清中氧化与抗氧化的平衡关系与伴胰岛素抵抗和胰岛β- 细胞分泌功能的研究不多,而且有一定的争议[5,6]。本研究通过检测氧化应激指标活性氧(ROS)、丙二醛(MDA)、总抗氧化能力(TAC)、超氧化物歧化酶(SOD)以及胰岛素抵抗指数(HOMA-IR)和胰岛 β 细胞分泌功能的变化,并通过稳态模型来评机体胰岛素抵抗及胰岛β细胞分泌功能的情况,探索氧化应激和 PCOS 胰岛素抵抗的关系,明确氧化应激在 PCOS 患者胰岛素抵抗发生发展与进程中的作用,为 PCOS 胰岛素抵抗的预防和治疗提供新的思路和方法。

1 资料与方法

1.1 研究对象

选取 2018 年 1 月至 2019 年 1 月于大连市妇幼保健院生殖保健中心就诊的 122 例患者进行研究。82 例 PCOS 患者作为研究组,诊断标准参照鹿特丹标准[7],具备以下 3 项中的 2 项即可诊断:(1)稀发排卵或无排卵;(2)经超声检查显示卵巢呈多囊样改变,即单侧卵巢有可见≥ 12 个直径 2～9 mm 的卵泡生成,和 / 或卵巢体积≥ 10 mL;(3)高雄激素血症或雄激素升高的临床表现,除外先天性肾上腺皮质增生、库欣综合征、分泌雄激素的卵巢或肾上腺肿瘤。根据胰岛素抵抗指数 HOMR-IR 把 PCOS 分为两组:胰岛素抵抗 IR 组 42 例和非 IR 组 40 例,同期选取单纯因男性因素不育而月经规律、内分泌激素正常的对照组患者 40 例,并排除其他内分泌疾病。所有患者在 3 个月之内未行任何药物治疗。该研究经我院伦理委员会批准,受试者均需签署相关的知情同意书。

1.2 收集样本

所有受试者均于月经周期第 2～4 天晨 8: 00 空腹抽静脉血测性激素、血糖、胰岛素水平,另抽 5 mL 静脉血肝素钠抗凝,2000 r/min 离心 10 min,收集上清夜置 -70℃低温冰箱中待检,以测定 ROS、MDA、TAC 和 SOD 水平。

1.3 标本检测

血清性激素和 FINS 采用化学发光法(美国 BECKMAN 公司仪器及试剂盒),FBG 采用糖氧化酶法,均由医院检验科完成;TAC 活性采用检测试剂盒 (江苏碧云天生物试剂公司)检测,人活性氧 ROS 采用 ELISA 试剂盒(武汉优尔生科技有限公司)检测,使用黄嘌检测化酶法检查血清 SOD,硫代巴比妥酸荧光法检测 MDA,试剂盒均购于南京建成生物工程公司。

1.4 胰岛素抵抗和胰岛β 细胞分泌功能评价

胰岛素抵抗 (HOMA) 用 HOMA 稳态平衡模式计算,HOMA-IR = FINS (μU/mL)× FBG(mmol/L) /22.5,胰岛 β 细胞分泌功能 HOMAβ=20× FINS (μU/mL)/[FBG(mmol/L) -3.5]。

1.5 统计学分析

数据采用 SPSS18.0 统计学软件包处理。计数资料采用 Chi-Square 检验,计量资料采用 t 检验,实验数据与临床评价指标间行相关性分析,用 Spearman 相关系数表示,P<0.05 认为差异有统计学意义。

2 结果

2.1 三组患者的一般情况比较

PCOS 胰岛素抵抗组患者的 BMI、LH、LH/FSH、T 显著高于非 IR 和对照组,差异有统计学意义(P<0.05),而三组年龄、E2、FSH 比较均无统计学差异(P>0.05),非 IR 组与对照组之间比较各指标测定均无统计学差异(P>0.05)(见表 1)。

表 1 三组患者基本临床资料比较($\bar{x}\pm s$)

Table 1 Comparison of the baseline clinical characteristics among three groups($\bar{x}\pm s$)

Groups	n	Age (year)	BMI (Kg/ m^2)	FSH (U/L)	LH (U/L)	LH/FSH	T (ng/mL)	E_2 (pgl/mL)
PCOS+IR	34	32.4± 2.7	26.1± 3.4*#	5.0± 1.1	9.6± 3.3*#	1.9± 0.5*#	0.7± 0.2*#	52.6± 10.4
PCOS+non-IR	32	30.8± 2.3	23.5± 2.7	5.4± 1.3	5.5± 1.8	1.1± 0.3	0.4± 0.1	43.3± 10.3
Control	32	32.2± 2.6	22.8± 2.5	5.2± 1.2	5.2± 1.6	1.0± 0.2	0.3± 0.1	39.6± 9.3

2.2 三组患者血清 sROS、MDA、TAC、SOD 含量比较

PCOS 胰岛素抵抗组血清 ROS 和 MDA 含量较非 IR 组显著升高(P<0.05),非 IR 组 ROS 含量显著高于对照组(P<0.05),而非 IR 组 MDA 和对照组相比差异无显著性(P>0.05);PCOS 胰岛素抵抗组血清 TAC 和 SOD 含量较非 IR 组和对照组显著降低(P<0.05),而非 IR 组血清 TAC 和 SOD 含量低于对照组,

但差异无显著性($P>0.05$)(见表 2)。

2.3 三组患者的胰岛素抵抗及胰岛 β 细胞功能评价

PCOS 胰岛素抵抗组患者的 FBG、FINS 和 HOMA-IR 显著高于非 IR 和对照组,而 HOMA-β 细胞分泌指数显著低于非 IR 和对照组,差异均有统计学意义($P<0.05$);非 IR 组与对照组之间比较各指标测定均无统计学差异($P>0.05$)(见表 3)。

表 2 三组患者氧化应激应激指标的比较

Table 2 Comparison of the Parameters of oxidative stress between three groups

Groups	n	ROS(ng/mL)	MDA(μmol/L)	TAC(mmol/L)	SOD(μU/L)
Control group	34	0.51± 0.32	9.6± 2.32	0.85± 0.38	80.2± 17.1
Non-IR group	32	1.02± 0.41*	10.31± 3.05	0.75± 0.29	74.3± 13.3
Group IR	32	14.52± 4.54*#	14.52± 4.54*#	0.52± 0.17*#	58.8± 10.4*#

表 3 胰岛素抵抗指数和胰岛 β 细胞分泌功能结果比较

Table 3 Parameters of HOMA-IR and pancreatic β cells secretory function

Groups	n	FBG(mmol/L)	FINS(μU/mL)	HOMA-IR	HOMA-β
Control group	34	4.5± 0.4	5.6± 0.5	1.2± 0.2	84.5± 8.6
Non-IR group	32	4.8± 0.5	6.8± 0.7	1.6± 0.3	78.2± 7.9
Group IR	32	6.5± 0.8*#	11.8± 0.9*#	2.8± 0.6*#	56.5± 7.2*#

2.4 PCOS 胰岛素抵抗组 HOMA -IR 和 HOMA-β 与各氧化应激指标之间的相关性

HOMA-IR 与 BMI 及血浆 MDA、ROS 呈显著正相关($P<0.05$),和血浆 TAC、SOD 呈显著负相关($P<0.05$)。HOMA-β 细胞分泌指数与血浆 TAC 呈显著正相关($P<0.05$),和 ROS 呈显著负相关($P<0.05$),与 BMI、MDA 及 SOD 无明显相关性($P>0.05$)(见表 4)。

表 4 HOMA -IR 和 HOMA-β 与各氧化应激指标之间的相关性分析

Table 4 Relationship between pancreatic β cells secretory function and oxidative stress

Indicators of oxidative stress	HOMA -IR	HOMA-β
BMI	0.245	-0.105
ROS	0.458	-0.626
MDA	0.347	-0.169
TAC	-0.514	0.582
SOD	-0.425	0.178

3 讨论

PCOS 是育龄期女性常见的内分泌异常的疾病，不同国家、种族、地区,个体其临床表现各不相同,呈现异质性和多态性[8]。根据 NIH 诊断标准,PCOS 发生在 6-10%的育龄妇女中,其主要内分泌特征表现为高雄激素血症、促性腺激素分泌变化、胰岛素抵抗等[9]。有报道显示在疾病早期,胰岛素抵抗就起着作用,与是否肥胖无关[10]。本研究结果显示 PCOS 胰岛素抵抗组患者的 BMI、LH、LH/FSH、T、FBG、FINS 和 HOMA- IR 均显著高于非 IR 和对照组，而 HOMA-β 显著低于非 IR 和对照组。而导致 PCOS 高雄激素血症发生的原因和以下两点相关,① 在 PCOS 胰岛素抵抗时,胰岛素会对垂体促黄体生成素产生刺激作用,促进其分泌并令卵巢功能增加,加速卵泡膜细胞增生,进一步刺激雄激素的合成和释放;② 胰岛素也对肝脏性激素结合球蛋白的合成具有抑制作用，可增加血中游离的雄激素,加速卵泡膜细胞合成分泌雄激素,继而刺激肾上腺雄激素的生成[11,12]。此外,高胰岛素血症还可促使芳香化酶对促卵泡生长素活性的增加,令颗粒细胞对促性腺激素刺激的敏感性得到增强,诱发 PCOS 患者出现排卵障碍[13,14]。

活性氧簇 ROS 是种有氧代谢的产物，主要作用是调控细胞凋亡、损伤修复、细胞增殖等信号传导途径,机体中 ROS 的表达过多可导致细胞胞膜出现脂质过氧化，改变膜流动性,增加机体氧化应激程度[15]。TAC 主要代表的是机体抵抗 ROS 的能力,有助于降低氧化脂质的产生,避免 ROS 的大量生成和聚集,防止细胞遭受到自由基损伤。如果 ROS/TAC 之间的平衡被打破,则代表氧化还原过程失衡,机体发生氧化应激反应状态,继而诱导细胞凋亡,造成组织器官损伤,诱发各类疾病产生[16]。MDA 属于脂质过氧化中的分解产物，其表达水平可了解机体脂质过氧化的严重程度,并间接了解细胞损伤程度[17,18]。SOD 是机体中作用关键的酶类抗氧化剂,具有清除生物体内自由基的作用,活力高低可以间接反映机体清除氧自由基的能力,可清除氧自由基保护细胞免受损伤同时及时修复受损细胞[19]。研究表明在氧化应激中,自由基、丙二醛(MDA)和其他脂质过氧化产物的产生均可能引起胰岛素抵抗[20]。

在许多疾病的发生发展中,氧化应激反应均占据重要地位[21]。已有研究显示氧化应激可启动肝脏损伤，是通过改变脂质、蛋白质和 DNA 含量以及控制基因转录和蛋白质表达、细胞凋亡和肝星状细胞活化的途径的实现的[22]。近几年来,有文献指出 ROS 在卵泡形成、卵巢发育、胚胎种植、妊娠期黄体等过程中均有着重要参与,与卵母细胞成熟度和胚胎发育潜能也可能有着直接关系[23]。研究证实多囊卵巢综合征女性存在氧化应激与是否肥胖和代谢紊乱无关,同时也可能是引起 PCOS 相关不孕的原因之一[24]。PCOS 女性中,氧化应激增加和炎症标志物如 C 反应蛋白(CRP)升高与肥胖和胰岛素抵抗风险增加有关[25,26]。

但也有研究认为氧化应激在 PCOS 不孕及其胰岛素抵抗中的作用是有争议的,Torun AN 等的研究显示与对照组相比,PCOS 患者的总氧化剂状态有所增加，但没有显著性差异[6]。Rains JL 发现 PCOS 患者和对照受试者中血浆硫代巴比妥酸反应物质水平,即脂质过氧化的副产物是相似的[27]。通过分析结果不同的原因和各研究在对 PCOS 患者及对照组的纳入标准上面不一,且对氧化应激标记物的选择、测量方法上面也不一样。在本研究中,已最大能力的控制可能出现的混杂因素,确定纳入标准和排除标准，例如不纳入和氧化应激、PCOS 相关的疾病等,并积极控制两组患者的年龄和不孕年限。

本研究结果显示与对照组相比,在 PCOS 的血浆中有明显异常氧化应激状态,PCOS 患者 ROS/TAC 显著高于正常对照组,提示 PCOS 患者血浆内处于高氧化应激水平,而在 PCOS 胰岛素抵抗组,这种异常表现的更为明显,即 ROS 产生显著增高,而抗氧化能力 TAC 显著下降．由此 ROS/TAC 更加失去平衡。PCOS 胰岛素抵抗组血清中 MDA 含量较非 IR 组显著升高，而非 IR 组 MDA 和对照组相比差异无显著性,PCOS 胰岛素抵抗组血清中 SOD 含量较非 IR 组和对照组显著降低,而非 IR 组血清 SOD 含量低于对照组,但差异无显著性。HOMA-IR 是反映机体胰岛素抵抗的重要检测方法，本研究结果显示 HOMA -IR 与 BMI 及血浆 MDA、ROS 呈显著正相关，和血浆 TAC、SOD 呈显著负相关。HOMA-β 细胞分泌指数与血浆 TAC 呈显著正相关，和 ROS 呈显著负相关，与 BMI、MDA 及 SOD 无明显相关性。提示 PCOS 胰岛素抵抗患者存在明显的氧化应激损伤，机体 ROS、MDA 生成过量，令 SOD、TAC 被过度消耗,诱发机体氧化和抗氧化状态的失衡,继而产生胰岛素抵抗。此外,机体发生氧化应激时线粒体是 ROS 的主要来源,既直接诱导 β 细胞的凋亡,又引起外周组织的胰岛素抵抗,而高胰岛素血症和 PCOS 相关的代谢并发症之间又有着密切联系[28,29]。胰岛素抵抗又通过多种途径可使 ROS 生成增多，加剧氧化应激,同时加重胰岛素抵抗,二者形成恶性循环,而且 PCOS 胰岛 β 细胞功能受损也与氧化应激有关[30]。肥胖程度越高,体内胰岛素抵抗、氧化应激异常越明显,推测在 PCOS 合并胰岛素抵抗的患者,尤其是肥胖型 PCOS 患者,体内极有可能也存在此种恶性循环的病理状态,胰岛素抵抗与高氧化应激状态互为因果。

总之,PCOS 患者的胰岛素抵抗和 HOMA-β 细胞分泌功能与体内的异常氧化应激状态有密切关系,深入研究氧化应激在 IR 中的作用机制,为临床预防、治疗 IR 提供新思路。且抗氧化治疗也可成为 PCOS 的新治疗策略,通过调节机体氧化 / 抗氧化的平衡,达到改善妊娠结局的作用。

参 考 文 献(References)

[1] Yau TT, Ng NY, Cheung LP, Ma RC. Polycystic ovary syndrome: a common reproductive syndrome with long-term metabolic consequences[J]. Hong Kong Med J, 2017, 23(6): 622-634

[2] Harris H R, Babic, Ana, Webb, Penelope M, et al. Polycystic ovary syndrome, oligomenorrhea, and risk of ovarian cancer histotypes: Evidence from the Ovarian Cancer Association Consortium [J]. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 2017, 27(2): 174-182

[3] Rocha A L L, Faria, L. C, Guimarães, T. C. M, et al. Non-alcoholic fatty liver disease in women with polycystic ovary syndrome: systematic review and meta-analysis [J]. Journal of Endocrinological Investigation, 2017, 40(12): 1-10

[4] Steller JG, Alberts JR, Ronca AE. Oxidative Stress as Cause, Consequence, or Biomarker of Altered Female Reproduction and Development in the Space Environment[J]. Int J Mol Sci, 2018, 19(12): 3729

[5] Papalou O, Victor VM, Diamanti-Kandarakis E. Oxidative Stress in Polycystic Ovary Syndrome [J]. Curr Pharm Des, 2016, 22 (18): 2709-2722

[6] Rajan R K, M., Siva Selva Kumar, Balaji, Bhaskar. Soy isoflavones exert beneficial effects on letrozole-induced rat polycystic ovary syndrome (PCOS) model through anti-androgenic mechanism [J]. Pharmaceutical Biology, 2017, 55(1): 242-251

[7] Zaremobini F, Kazemi A, Farajzadegan Z. A comprehensive mental health care program for women with polycystic ovary syndrome: Protocol for a mixed methods study [J]. Reproductive Health, 2018, 15 (1): 46

[8] Teede H J, Misso Marie L, Costello Michael F, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome [J]. Clinical Endocrinology, 2018, 40(04): 188-195

[9] Htet T D, Teede H J, De Courten B, et al. Asthma in reproductive-aged women with polycystic ovary syndrome and association with obesity [J]. European Respiratory Journal, 2017, 49(5): 1601334

[10] Al-Jefout M, Alnawaiseh, Nedal, Al-Qtaitat, Aiman. Insulin resistance and obesity among infertile women with different polycystic ovary syndrome phenotypes[J]. Scientific Reports, 2017, 7(1): 5339

[11] Teede HJ, Hutchison SK, Zoungas S. The management of insulin resistance in polycystic ovary syndrome [J]. Trends Endocrinol Metab, 2007, 18(7): 273-279

[12] Liu A L, Xie, Hui Jun, Xie, Hong Yan, et al. Association between fat mass and obesity associated (FTO) gene rs9939609 A/T polymorphism and polycystic ovary syndrome: a systematic review and meta-analysis[J]. Bmc Medical Genetics, 2017, 18(1): 89

[13] 陈子江. 人类生殖与辅助生殖 [M]. 北京: 科学出版社,2005: 146-150

[14] Alexiou E, Hatziagelaki, Erifili, et al. Hyperandrogenemia in women with polycystic ovary syndrome: prevalence, characteristics and association with body mass index[J]. Horm Mol Biol Clin Investig, 2017, 29(3): 105-111

[15] Maktabi M, Chamani, Maryam, et al. The Effects of Vitamin D Supplementation on Metabolic Status of Patients with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial

[J]. Hormone & Metabolic Research, 2017, 49(07): 493-498

[16] Palomba S, Daolio, Jessica, et al. Oocyte Competence in Women with Polycystic Ovary Syndrome [J]. Trends in Endocrinology & Metabolism, 2017, 28(3): 186-198

[17] Jin J, Ruan, Xiangyan, et al. Prevalence of diminished ovarian reserve in Chinese women with polycystic ovary syndrome and sensitive diagnostic parameters [J]. Gynecological Endocrinology the Official Journal of the International Society of Gynecological Endocrinology, 2017, 33(9): 1

[18] Imai Y, Kuba K, Neely GG, et al. Penninger JM. Identification of oxidative stress and Toll-like receptor 4 signaling as a key pathway of acute lung injury[J]. Cell, 2008, 133(2): 235-249

[19] Behboudi-Gandevani S, Ramezani Tehrani, F, Bidhendi Yarandi, R, et al. The association between polycystic ovary syndrome, obesity, and the serum concentration of adipokines [J]. Journal of Endocrinological Investigation, 2017, 40(8): 1-8

[20] Rezvan N, Moini A, Janani L, et al. Effects of Quercetin on Adiponectin-Mediated Insulin Sensitivity in Polycystic Ovary Syndrome: A Randomized Placebo-Controlled Double-Blind Clinical Trial[J]. Hormone & Metabolic Research, 2017, 49(02): 115-121

[21] Brüggmann, Dörthe, Berges, Lea, Klingelhöfer, Doris, et al. Polycystic ovary syndrome: analysis of the global research architecture using density equalizing mapping [J]. Reproductive Biomedicine Online, 2017, 34(6): 627

[22] Anastasiou O E, Canbay, Ali, Fuhrer, Dagmar, et al. Metabolic and androgen profile in underweight women with polycystic ovary syndrome [J]. Archives of Gynecology & Obstetrics, 2017, 296 (2): 363-371

[23] Yao K, Bian, Ce, Zhao, Xia. Association of polycystic ovary syndrome with metabolic syndrome and gestational diabetes: Aggravated complication of pregnancy (Review)[J]. Experimental & Therapeutic Medicine, 2017, 14(2): 1271-1276

[24] Reid S P, Kao C N, Lauri Pasch. Ovarian morphology is associated with insulin resistance in women with polycystic ovary syndrome: a cross sectional study[J]. Fertility Research & Practice, 2017, 3(1): 8

[25] Penzias A, Bendikson, Kristin, et al. Role of metformin for ovulation induction in infertile patients with polycystic ovary syndrome (PCOS): a guideline[J]. Fertility & Sterility, 2017, 108(3): 426-441

[26] Chitme H R, Al Azawi, Eman A.K, et al. Anthropometric and body composition analysis of infertile women with polycystic ovary syndrome [J]. Journal of Taibah University Medical Sciences, 2017, 12 (2): 139-145

[27] Reis G V O P D, Gontijo N A, Rodrigues K F, et al. Vitamin D receptor polymorphisms and the polycystic ovary syndrome: A systematic review: Vitamin D and PCOS[J]. Journal of Obstetrics & Gynaecology Research, 2017, 43(3): 436-446

[28] Jacob S L, Field H P, Calder N, et al. Anti-Mü llerian Hormone reflects the severity of Polycystic Ovary Syndrome [J]. Clinical Endocrinology, 2017, 86(3): 395-400

[29] Ahmadi S, Jamilian, Mehri, et al. Probiotic supplementation and the effects on weight loss, glycaemia and lipid profiles in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial[J]. Human Fertility, 2017, 20(4): 1

[30] Tosi F, Bonora E, Moghetti P. Insulin resistance in a large cohort of women with polycystic ovary syndrome: a comparison between euglycaemic-hyperinsulinaemic clamp and surrogate indexes [J]. Human Reproduction, 2017, 32(12): 1-7

(上接第 4710 页)

[23] 骆峰, 王明松, 陆善伟, 等. 单操作孔胸腔镜对高龄孤立性肺结节的疗效及对其肺功能和预后的影响[J].海南医学院学报, 2018, 24 (23): 2090-2093

[24] Li C, Liu B, Jia H, et al. Computed tomography-guided hook wire localization facilitates video-assisted thoracoscopicsurgery of pulmonary ground-glass nodules [J]. Thorac Cancer, 2018, 9 (9): 1145-1150

[25] Huang S, Cao X, Li J, et al. Analgesic effect of flurbiprofen axetil in treatment of single hole thoracoscopic surgery for pneumothorax [J]. Pak J Pharm Sci, 2017, 30(5(Special)): 1875-1882

[26] Wang X, Wang L, Zhang H, et al. Feasibility and application of single-hole video-assisted thoracoscope in pulmonary peripheral tumors [J]. Oncol Lett, 2016, 12(6): 4957-4960

[27] Abd-Elshafy SK, Abdallal F, Kamel EZ, et al. Paravertebral Dexmedetomidine in Video-Assisted Thoracic Surgeries for Acute and Chronic Pain Prevention[J]. Pain Physician, 2019, 22(3): 271-280

[28] Karmy-Jones R. Commentary on "Large traumatic pneumato cele treated using video-assisted thoracoscopic surgery" [J]. J Trauma Acute Care Surg, 2019, 86(6): 1041

[29] Zhang LB, Wang B, Wang XY, et al. Influence of video-assisted thoracoscopic lobectomy on immunological functions in non-small cell lung cancer patients[J]. Med Oncol, 2015, 32(7): 201

[30] Mei J, Guo C, Xia L, et al. Long-term survival outcomes of video-assisted thoracic surgery lobectomy for stage I-II non-small cell lung cancer are more favorable than thoracotomy: a propensity score-matched analysis from a high-volume center in China[J]. Transl Lung Cancer Res, 2019, 8(2): 155-166